

REMARKS

Claims 2-3, 5-6, and 8-11 have been amended and claims 18-23 have been added herein. Claims 1-11 and 18 appear in this application for the Examiner's review and consideration. Claims 12-17 have been cancelled without prejudice to applicants' right to file a divisional applications for those claims. The amendments and new claims are fully supported by the original claims and by the specification. New claims 18-23 are directed to preferred features of the invention. Also, new claim 18 is also supported by the specification, for example at page 5, last paragraph.

The specification has also been amended at page 2, first paragraph after the heading "SUMMARY OF THE INVENTION." The amendment to the specification is fully supported by the original claims 5 and 10, and original claim 4 of the priority document, Application No. 99108717.2, filed April 30, 1999 in the European Patent Office under 35 U.S.C. § 119. No new matter has been added.

Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set for on pages 2-5. Applicants traverse.

Applicants' invention as presently claimed is not limited to and does not require only the specific strains disclosed in the specification, for example at page 10, as cited by the Examiner. The presently claimed invention pertains to a medium for growing Lactobacilli. The strains mentioned on page 10 of the specification are not components of the medium, but simply typical examples of *Lactobacilli* that have been successfully grown on Applicants' medium. A wide range of other *Lactobacilli* strains are readily available to the public, and applicants have no reason to believe that they will behave any differently on their new medium. For these reasons, the specific strains disclosed are not essential to the claimed invention or its use. Because the strains on page 10 of the specification are not essential to the claimed medium, it is not necessary to show the strain have been deposited or to provide an affidavit or declaration stating that the specific strain will be released to the public without restriction.

Claim 5 is rejected under 35 U.S.C. § 112, first paragraph, for reasons set forth on page 5 of the Office Action.

Applicants have herein amended the specification to include the addition of iron in an amount ranging from about 10 to 200 mg/l. This amendment is fully supported by the language of the originally filed claims as indicated above. Claim 5 is therefore supported by the specification and the rejection is overcome.

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Claims 2-6 and 8-11 are rejected under 35 U.S.C. § 112, second paragraph, for the reasons set forth on page 5-7 of the Office Action.

Applicants have amended claims 2-6 and 8-11 as suggested by the Examiner and therefore request that this rejection be withdrawn.

Claims 1-11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gil *et al.*, U.S. Patent No. 4,544,559, in view of Hata, U.S. Patent No. 4,879,238. Applicants traverse.

The invention as presently claimed relates to a medium for growing *Lactobacilli* comprising a milk-derived base and an additive system that comprises at least four amino acids, at least two ribonucleotide precursors, and iron, in amounts sufficient to promote the growth of *Lactobacilli*.

One of the problems solved by the present invention is that while Applicants' medium supports the growth of *Lactobacillus* strains, the medium avoids problems associated with prior art media. Many of the prior art media are very complex and often cause an "off-flavor" in the food products produced using *Lactobacillus* grown thereon. In addition, many of the prior art media were developed for growing specific strains of lactic acid bacteria and remain undefined as to the exact constituents added. The shortcomings of the prior art media render them inappropriate and economically unsuitable for industrial manufacture of food products in general and dairy products in particular. Applicants' presently claimed invention is well suited for use in the manufacture of dairy products, not causing "off-flavors," is made of simple constituents, and is cost effective, while providing the nutrients need for growth of many *Lactobacillus* strains. These are unexpected benefits that support the patentability of the presently claimed medium.

Gil *et al.* relates to a "humanized" milk formulation for infant nourishment, *i.e.*, a milk which has been artificially treated to become similar to human milk (column 1, lines 57-59). For this purpose specific nucleotides are added to the formulations of Gil *et al.* which are supposed to enable the establishment of an intestinal microflora and a serum fatty acids pattern similar to those found in breast-fed infants (column 9, lines 47-49).

An important difference between the milk formulation of Gil *et al.* and Applicants' presently claimed medium is that the milk formulation of Gil *et al.* is supplemented with nucleotides (AMP, CMP, GMP, IMP and UMP (column 9, lines 39), while Applicants claimed medium is supplemented with "ribonucleotide precursors." The definition of the term "ribonucleotide precursors" is defined as "free bases such as adenine,

guanine, cytosine, thymine, and uracil," at page 4, third paragraph of the present specification, components that are quite different from those disclosed in Gil *et al.*

Gil *et al.* also fails to mention the addition of at least four amino acids. Furthermore, Gil *et al.* is in general directed to a different subject matter having a different purpose, an attempt to mimic "human milk" for the consumption of infants. In contrast, Applicants' *Lactobacilli* medium as claimed is intended to be useful in growing many strains of *Lactobacilli* in a cost effective and industrial useful way for use in the manufacture of food products, particularly those that are milk based, such as dairy products.

Hata fails to remedy the deficiencies of Gil *et al.*. Hata teaches the deodorization of excrements (a mixture of feces and urine), using microorganisms (column 2, lines 11-15 and column 5, line 11). The examiner relies on Hata as teaching that amino acids are useful for growing *Lactobacilli*.

First, Hata fails to even mention *Lactobacilli*, which are bacteria forming lactic acid starting from carbohydrates and lactic acid, being in general gram-positive and mainly having complex nutritional requirements. Hata, in contrast, is specifically directed to autotrophic bacteria (column 4, lines 28-33). The autotrophic bacteria in Hata are capable of synthesizing their own organic substances from inorganic compounds, and in particular to the gram-negative strains listed in Table 2 (Columns 7-8).

Second, the amino acids listed in columns 13 and 14, of Hata are "amino-acids which are effective to keep the deodorizing power of the bacteria at almost constant level for many generation . . ." Hata is directed to a excrement based medium, which is extremely different from applicants food or milk based medium. Furthermore, there is no suggestion in Hata that at least four amino acids should be added, either to his materials to be deodorized or to applicants' milk based *Lactobacilli* medium to promote the cultivation of *Lactobacilli* strains therein.

Applicants' *Lactobacilli* medium is not taught or suggested by Gil *et al.* alone or in view of Hata. Furthermore, there is no motivation to combine the teachings of Gil *et al.*, relating to a humanized milk formulation, with Hata, relating to the deodorization of excrements. Applicants' therefore respectfully request that the rejection be withdrawn.

Claims 1-11 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Gil *et al.* Applicants traverse.

The invention as presently claimed relates to a medium for growing *Lactobacilli*, comprising a milk-derived base and an additive system that comprises at least

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four amino acids, at least two ribonucleotide precursors, and iron, in amounts sufficient to promote the growth of *Lactobacilli*.

As stated above, Gil *et al.* relates to a "humanized" milk formulation for infant nourishment, *i.e.*, a milk which has been artificially treated to become similar to human milk (column 1, lines 57-59). Gil *et al.* fails to teach the addition of at least two "ribonucleotide precursors" and the addition of at least four amino acids to a milk-based *Lactobacillus* medium for the purpose of promoting the growth of *Lactobacilli* in a cost effective and industrial useful way. Based on these deficiencies, Gil *et al.* can not anticipate Applicants' invention as claimed. Furthermore, there is nothing in Gil *et al.* to suggest or motivate one to make Applicants' *Lactobacillus* medium with at least two ribonucleotide precursors and at least four amino acids. Therefore, Applicants' invention as presently claimed is not obvious and this rejection should be withdrawn.

In view of the foregoing, it is believed that the entire application is now in condition for allowance, early notice of which would be appreciated. Should any issues remain, a personal or telephonic interview is respectfully requested to discuss the same in order to expedite the allowance of all the claims in this application.

No fees are believed to be due for the claim changes made in this response. Should any fees be due, however, please charge them to Winston & Strawn Deposit Account No. 501-814.

Respectfully submitted,



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APPENDIX A
MARKED COPY OF REPLACEMENT PARAGRAPH IN THE SPECIFICATION

On page 2, please replace the first paragraph after the heading "SUMMARY OF THE INVENTION" starting with "The present invention solves" with the following replacement paragraph:

"The present invention solves the shortcomings of the art by providing a medium for the growth of *Lactobacillus* strains. The medium comprises a milk-derived base that has been supplemented by an additive system that includes at least four amino acids, at least two ribonucleosides or other ribonucleotide precursors, and beneficially iron. These components are added in amounts sufficient in combination to promote growth of *lactobacilli* in the medium. The specific amount of each of the ribonucleotide precursors, *i.e.*, free bases, ribonucleosides, and deoxyribonucleosides, to be added to the base lie in the range from about 10 to about 500 milligrams per liter (mg/l) base, preferably from about 10 to about 100 mg/l base. Preferably, iron is added to the base in an amount ranging from about 10 to about 200 mg/l and more preferably [In a preferred embodiment iron is added to the base] in an amount from about 50 to about 100 mg/l milk."

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APPENDIX C

MARKED COPY OF AMENDED CLAIMS

2. (Amended) The medium according to claim 1, wherein the ribonucleotide precursors are ribonucleosides, each added in the range of from about 10 to about 500 milligrams per liter of the medium.
3. (Amended) The medium according to claim 1, wherein the ribonucleotide precursors are selected from the group consisting of adenosine, guanosine, cytidine, and uridine, and wherein the at least four amino acids added comprise cysteine.
5. (Amended) The medium according to claim 1, wherein the amount of iron added is in the range of about 10 to 200 milligrams of iron per liter of the medium.
6. (Amended) The medium according to claim 1, wherein the at least four amino acids added comprise cysteine, alanine, serine and isoleucine, each in an amount ranging from about 10 to about 200 milligrams per liter of the medium.
8. (Amended) The medium according to claim 7, wherein the compound that provides antioxidant or reducing activity is selected from the group consisting of cysteine, thioglycollic acid, ascorbic acid, [or] and mixtures thereof.
9. (Amended) The medium according to claim 1, further comprising added magnesium and aspartic acid, and wherein the ribonucleotide precursors comprise free bases.
10. (Amended) The medium according to claim 9, wherein the at least four amino acids added comprise cysteine, alanine, serine and isoleucine, each in an amount ranging from about 10 to about 200 milligrams per liter of the medium; wherein the ribonucleotide precursors added are each in the range of from about 10 to about 500 milligrams per liter of the medium; and wherein the [amount of] iron added [in the additive system is sufficient to add] is in the range of about 10 to about 200 milligrams [of iron] per liter of the medium.

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11. (Amended) The medium according to claim 1, wherein the milk-derived based comprises whole milk, partially de-fatted milk, skim milk or [UHT] ultra-high temperature pasteurized milk, whether the mild-derived base is prepared from natural sources or from dried milk powder by addition of water.